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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,616	02/15/2002	Martin P. Redmon	4821-464	2810

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EXAMINER
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ART UNIT	PAPER NUMBER
1615	7

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/075,616	Applicant(s) REDMON ET AL.	
	Examin r Lakshmi S Channavajjala	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-40 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of declaration dated 5-13-02, IDS dated 4-10-02, second IDS dated 2-15-02 and Letter dated 2-15-02, is acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-6, and 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woosley et al.

WO teaches a pharmaceutical composition comprising norastemizole, a derivative of astemizole, for the treatment of allergic disorders such as allergic rhinitis (page 4, lines 1-8), with and without lactose. Claim 2 requires lactose-free formulations. Example 4 of WO does not contain lactose. The compositions of WO are free of mono and disaccharides. The treatment comprises administration of norastemizole in an amount of 1-200 mg, as claimed in the instant invention, in a pharmaceutically acceptable carrier or excipient (page 6, lines 7-13). WO also teaches various routes and dosage forms for the administration of norastemizole (page 9, lines 33-39). In addition, WO teaches excipients such as binders, diluents, disintegrants, lubricant etc., are also disclosed in the solid pharmaceutical norastemizole composition (page 10, lines 24-32 and examples 4 and 5 on page 16). The formulations exemplified by WO also teach lower concentrations of STARCH 1500 and magnesium stearate. WO does not teach the limitation,

"wherein diluent, lubricant, disintegrant and binder are not same". However, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the appropriate excipients without sacrificing the therapeutic effect of norastemizole. Further, in the absence of any undesirable effect in using the same material for performing different functions, choosing an appropriate combination of excipients would have been within the scope of a skilled artisan.

2. Claims 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over (WO 94/07495) (hereafter WO) in view of Blaug et al and Castello et al.

WO teaches norastemizole formulations with and without the presence of lactose. WO does not specifically recognize the incompatibility of norastemizole and lactose-based excipients.

Blaug et al and Castello et al teaches formulations containing amine salts, lactose and other sugars and degrade rapidly due to the amine base-carbonyl interaction, in particular in the presence of high heat and moisture. The amine base is released due to a reaction of the alkaline lubricant such as magnesium stearate, which in turn form stearic acid, furnishing alkaline medium in the adsorbed moisture. Although Blaug et al and Castello et al does not specifically teach norastemizole formulations containing lactose, and as applicants also disclose in the instant specification that norastemizole is an amine containing compound (chemical name is N-(4-piperidynyl)-1H-benzimidazole-2-amine is sensitive to amine-base-carbonyl-interaction. Therefore, a skilled artisan possessing the teachings of Blaug et al and Castello et al would expect degradation of norastemizole in the presence of lactose, lubricants such as magnesium stearate, and factors such as high

humidity and temperature. Therefore, it would have been obvious for a skilled artisan at the time of the instant invention to eliminate lactose and other sugars from the formulations containing amines as active ingredients or to carefully optimize the amounts of various excipients such as magnesium stearate, lactose and other sugars, and also control the moisture, temperature of the formulation so as to avoid degradation of norastemizole. Alternatively, an anhydrous composition containing lactose would still have been obvious because in the absence of water, lactose does not cause degradation of norastemizole.

3. Claims 9-13, 22-24, 29-32 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woosley et al (WO 94/07495) (hereafter WO) further in view of Remington: The science and practice of Pharmacy (Remington's).

The teachings of WO discussed above, does not contain claimed croscarmellose sodium and microcrystalline cellulose.

Remington's teaches oral dosage forms such as tablets, capsules etc., dosage forms and the addition of various additives or excipients that help in the preparation of the dosage forms, such as lubricants, diluents, binders and glidants or those that impart additional physical characteristics to the tablets such as disintegrants, colors, flavors, etc. Among the first group, Remington's teaches kaolin, calcium sulfate, dry starch, microcrystalline cellulose etc (as diluents, page 1617); gelatin, sugars, gum, cellulose derivatives, PVP etc (as binders, page 1617); lubricants talc, oils, magnesium stearate, aluminum stearate, PEG, etc., (as lubricants, page 1618) and croscarmellose sodium,

sodium starch glycollate etc., (as disintegrants (page 1619). Particularly, Remington's teaches croscarmellose sodium as a super disintegrant, which is effective as it swells 4 to 8 fold in less than 10 seconds, followed by sodium starch glycolate that swells 7 to 12 fold in <30 seconds. It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the appropriate excipients with an expectation to achieve the desired properties for preparing dosage forms or physical properties. Further, optimizing the amounts f the additives for their art recognized effect would have been within the scope of a skilled artisan.

4. Claims 7, 8, 14- 21 and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woosley et al (WO 94/07495) (hereafter WO) in view of Remington's and Gilis et al.

WO and Remington's teachings have been discussed above. The cited references do not teach coated particles of norastemizole.

The teachings of WO and Remington's have been discussed above. WO teaches norastemizole powders or granules (page 11), which read on particles. Examiner notes instant claims do not state any particular size of the particles. However, the references do not teach coated norastemizole.

Gilis et al teaches extended release of astemizole in film-coated tablets for the treatment of allergic disorders such as allergic rhinitis (column 1, lines 11-34), in particular micronized astemizole (col.3, lines 10-13). Gilis also teaches a combination of an antihistamine and a decongestant such as pseudoephedrine in the composition. In

order to avoid contact of the medicament with water vapor, Gilis et al teaches the packaging of coated tablets into blister packs (column 4, lines 40-43). Gilis teaches astemizole preparation coated with film forming polymers for extended release and teaches the claimed polymers in col. 2-col. 3. In particular, see col. 3, lines 10-37.

Gilis does not teach norastemizole and only teaches astemizole. However, WO recognizes both astemizole and norastemizole are equally effective in their therapeutic activity and norastemizole lacks the adverse effects of astemizole. Therefore, it would have been obvious for a skilled artisan to choose norastemizole-containing composition of WO and coat with film-forming polymers of Gilis because the polymers of Gilis provide extended release of norastemizole and thus avoids repeated administration of the drug.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7921 for regular communications and 703-308-7921 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Lakshmi Channavajjala
Patent Examiner
Art Unit 1615
June 24, 2003